REMARKS/ARGUMENTS

Applicants thank the Examiner for the considered response and explicit prior art references. Claims 1 and 4 have been amended. Claims 1 - 6 and remain in the case. Reconsideration of the patent application is respectfully requested in view of the foregoing amendments and following remarks

The instant invention is drawn to a PTFE suture, graft or suture/graft combination having a polymer coating containing releasable biological agents for the reduction of smooth muscle cell proliferation in a sutured, grafted or injured area of a vessel or arterial wall.

Claim 1 as amended recites "A suture, graft or suture/graft combination comprising PTFE and having a polymer coating containing releasable biological agents for the reduction of smooth muscle cell proliferation and prevention and reduction of intimal hyperplasia and in a sutured, grafted, or injured area of a vessel or arterial wall."

Amended claim 4 calls for "A suture, graft or suture/graft combination comprising PTFE having a reservoir containing releasable biological agents for the reduction of smooth muscle cell proliferation and prevention and reduction of intimal hyperplasia, in a sutured, grafted area or injured area of a vessel or arterial wall, said biological agent being osmotically released through the pores in the reservoir."

The amended claims also recite the reduction of intimal hyperplasia. None of the cited references teaches this feature of the instant invention. Applicants have observed long-term restenosis and intimal hyperplasia in surgical patients and attribute it to the inefficient delivery of the coated drugs. The adhesion of the drugs to and delivery from smooth-walled surfaces of devices is thought to be erratic and inefficient over long periods, although short term effects may be similar in reducing SMC and the like.

Claim Rejection 35 U.S.C. §112 #1:

Claims 1-6 are rejected under 35 U.S.C. §112, 1st paragraph.

Examiner argues that while *reduction* of SMC proliferation and intimal hyperplasia are known in the art, *prevention* is not known and has not been clinically established.

Examiner appears to believe that when tissue cells are damaged during surgery (a) SMC proliferation and intimal hyperplasia inevitably occur and (b) that the presence of drugs results in the *reduction* of hyperplasia in a subsequent step. This is contrary to the current state of knowledge in the art. It is widely known that smooth cell production and proliferation causes intimal hyperplasia in the injured vessel. Thus reduction in SMC proliferation would implicitly prevent intimal hyperplasia and thereby reduce its formation.

Applicants contend that the drugs act on the injured tissue cells; the action of the claimed drugs is to reduce or inhibit SMC proliferation and ***consequently*** prevent intimal hyperplasia. Applicants do not claim ***suppression*** of intimal hyperplasia *ab initio*. Stated differently, *prevention* is an inherent function of the drug that further leads to *reduction* of intimal hyperplasia. More explicitly, reduction of intimal hyperplasia occurs by preventing its formation and not by its shrinkage or removal after it is formed.

Applicants argue that the superior osmotic elution of the drugs from the instant porous sutures and the controlled diffusion from the polymer coated sutures result in a greater degree of preventive action than can be expected from commercially available sutures or grafts comprising smooth-walled materials.

Applicants request the withdrawal of the §112 rejection in view of the amendments and the clarification offered above. Claims 1 and 4 are amended.

Claim Rejection 35 U.S.C. §103(a):

Claims 1 -3 and 4-6 have been rejected under 35 U.S.C. §103(a) as being anticipated by Shibuya (USPGPUB 2002/0055759, "Shibuya") in view of US Pat. No. 6,918,69 to Shaw et al. ("Shaw") **[A - What's the correct #?]**

Shibuya discloses a surgical suture coated with one or more biologically active compounds. Shibuya also discloses a method of making a coated suture, placing the coated suture in an organism, and a method of using the coated suture in the treatment of diseases, such as cancer. Biologically active compounds that may be used include antibiotics, antifungal, anti-viral, anti-microbial compounds and the like (col. 5, paragraph 0038).

The Shibuya reference is directed to an entirely different process in the art. The Shibuya reference teaches a method of coating "a biologically active compound on a suture" (p. 2, paragraph 0013). Shibuya does not teach the instant suture material, PTFE, recited in the amended independent claims 1 and 4. Shibuya has no reference whatsoever to grafts or suture/graft combinations recited in instant claims 1 and 4. Shibuya does not teach plasma coating the suture with a polymer as recited in claim 2. In fact Shibuya coats Interleukins and the like directly on the suture material from solution -- with no plasma coated polymer. While the biological compounds of Shibuya are alleged to be curative, they do not prophylactically reduce smooth muscle cell proliferation as recited in the instant claims. Shibuya does not address reduction of intimal hyperplasia, the mechanism of which, as argued above, is different from administering drugs to cancer cells cited in Shibuya's examples. Shibuya does not teach "a reservoir containing releasable biological agents" as recited in claim 4. It does not teach "rapamycin, taxol, derivatives of taxol and rapamycin, and combinations thereof" as recited in claims 3 and 5. These drugs are particularly targeted to reduce SMC proliferation and intimal hyperplasia and belong to a different class from those listed by Shibuya and cited by Examiner.

Shaw's invention is directed to a mode of delivering biological agents locally with implanted medical devices. Shaw's broad disclosure encompasses diverse devices all characterized by two opposing ends and a middle; primary examples are stents. The devices are used in a wide range of therapies including radiotherapy, cryotherapy, DNA therapy and the like. A plethora of broad classes of drugs and biologically active coatings is also prescribed. Among the alleged benefits of local drug delivery is mitigation of hyperplasia in vascular procedures.

The instant invention narrowly claims porous PTFE sutures with specific biological coatings for reduction of intimal hyperplasia and inhibition of SMC proliferation.

Applicants believe, respectfully, that Examiner's deft use of the term "graft" is disingenuous. As stated by the Examiner in the §112 rejection, the relative skill of those in the art is high. One of such skill would be able to distinguish between (smooth) grafts used to cover the ends of implanted devices such as stents and catheters as disclosed in Shaw (col. #13, 55-67) from those recited in the instant disclosure wherein the suture or graft is placed *directly over injured vessels* to deliver drugs locally (p.8, lines 10-20). The porous structures of the instant grafts and sutures may not provide the smooth abrasion-lowering characteristics required for Shaw's application. This is also apparent from Shaw's use of the term "graft" (col. #13; lines 65-67) in quotes suggesting an unconventional use of the term for strips of polymers and sutures woven together at the ends of a stent. Applicants agree and state in the disclosure that devices coated with biologically active agents are known in the art and include sutures and grafts. These are known, smooth-walled materials which do not hold or deliver the drugs as efficaciously as the instant claimed sutures and grafts. Further, neither Shibuya nor Shaw teaches a *PTFE suture or graft or suture/graft combination with a polymer coating* which carries the biologically active drug as recited in claim 1. They do not teach delivering drugs from a *reservoir* on the sutures or grafts as claimed in claim 4.

Examiner's contention that one would be motivated to use e-PTFE (expanded PTFE) as taught by Shaw in Shibuya's sutures is unconvincing and an improper combination derived from the instant disclosure. As argued above, Shaw's sutures, designed to minimize abrasion, are not as effective as the instant polymer-coated sutures or reservoir-bearing grafts and sutures. Further abrasion is not a consideration in the use of sutures and thus there would not be motivation to reduce abrasion by substituting PTFE in Shibuya's sutures.

The combination of Shibuya and Shaw would not lead to the instant invention since neither teaches polymer-coated PTFE (instant claim 1) or a drug-bearing reservoir on PTFE (claim 4).

Examiner contends that the limitation "plasma-assisted coating" (instant claim 2) is a future-intended use limitation that adds no patentable weight to the claim. Applicants vigorously disagree.

The instant claims are directed to an article of manufacture; viz., a PTFE-suture coated with a polymer that carries biologically active agents. As disclosed by Applicants (p.12, lines 8-16), plasma-assisted coatings provide for complex drug delivery strategies that other coating techniques do not. This is a critical feature of the instant invention. In addition to being able to regulate drug delivery through altered surface chemical activity and the like, plasma assisted coatings provide uniform, thin coatings of controlled thickness. Applicants have recognized the versatile properties of plasma assisted coatings and have adopted them for their drug delivery on sutures and grafts.

Applicants once again agree that there are diverse drug-eluting sutures and grafts, as disclosed by Shibuya and Shaw (above) and numerous methods of providing the drug coating on the sutures and grafts. The instant sutures and grafts comprising PTFE with plasma-assisted polymer coating are not taught or suggested either individually or in combination by the references cited. For these reasons, instant claims 1-6 are allowable.

Claims 1-6 have been rejected under 35 U.S.C. §103(a) as being obvious over U.S. Pat. No. 6,890,546 to Mollison et al. (Mollison) in view of Shaw and again over U.S. Pat. No. 6,919,100 to Narayanan in view of Shaw.

These rejections suffer from the same deficiencies argued above.

The primary references do not teach a PTFE-suture or graft. The motivation for incorporating Shaw's PTFE (which is used to cover the ends of stents and catheters and thereby provide a smooth abrasion-free insert) is not tenable in the case of bare sutures and grafts which are placed directly over injured body lumen. It is not clear to the Applicants that the smooth-walled PTFE required for Shaw's application would provide the same efficacy of a porous PTFE carrier which may further carry a polymer coating or a reservoir. Neither the primary references nor Shaw teaches a plasma-assisted polymer coating on the PTFE suture or graft. Thus, even if one were to substitute the sutures and grafts of the primary references with PTFE, it would not lead to the instant invention.

For these reasons Applicants respectfully request the withdrawal of all the rejections and allowance of claims 1-6.

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